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Synthetic Organic Chemicals

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The Fries Reaction

THE rearrangement of aryl esters of carboxylic acids to hydroxyaryl ketones by heating with aluminum chloride was first investigated by Fries and Finck. They converted several esters of chloroacetic acid into the corresponding hydroxy-ω-chloroacetophenones. This original work is described in Berichte *41*, 4371 (1908). Rosenmund and Schnurr in Ann. *460*, 56 (1928) found recently that the reaction proceeds much more rapidly, and in many cases with improved yields, if carried out in nitrobenzene solution.

The position taken by the migrating group is greatly influenced by the temperature. Thus, when m-cresyl acetate is treated with aluminum chloride in nitrobenzene at room temperature, an 80% yield of the p-hydroxy ketone results, while at 165°, a 95% yield of an ortho isomer is obtained. At 90° the quantities of the two ketones formed are nearly equal. m-Cresyl benzoate behaves similarly. There is, however, some tendency for the esters of a higher molecular weight acid to give a considerable amount of ortho hydroxy ketone even at low temperatures. This is shown by Baltzly and Bass in J. Am. Chem. Soc. *55*, 4292 (1933). The directive influence of the methyl group varies with its position, o-cresyl benzoate on isomerization giving more of the p-hydroxy ketone than does m-cresyl benzoate under like conditions. The separation of ortho and para hydroxyaryl ketones is generally very easy because of the much lower boiling point of the ortho isomer due to chelation of the hydroxy and keto groups. These hydroxyphenyl alkyl ketones obtained by the Fries reaction are convenient intermediates for the preparation of alkylphenols which result from the reduction of the ketones with amalgamated zinc and hydrochloric acid. This reaction is described by Coulthard, Marshall, and Pyman in J. Chem. Soc. *280* (1930).

A number of interesting syntheses have been carried out which involve the esters of polyhydroxy phenols. The diacetate of catechol was found by Rosenmund and Schnurr to give 3,4-dihydroxyacetophenone, one acetyl group being split off from the molecule probably as acetyl chloride. If equimolecular quantities of catechol and the diacetate were mixed and then treated with aluminum chloride in nitrobenzene solution, the catechol was also converted into the ketone. Other polyhydroxy compounds have recently been studied by Mauthner, and their reactions described in J. Prakt. Chem. *118*, 314 (1928); *136*, 205, 213 (1933).

In some instances where the aryl ester contains several methyl groups, these may migrate during the Fries transformation. Auwers and co-workers have studied and reported the effect of the position of various alkyl groups in

Annalen, *447*, 162 (1926); *460*, 240 (1928); *483*, 44 (1930). The ethyl group is displaced more readily than methyl, and if ethyl groups are present in both ortho and para positions, the ortho group is the one which migrates.

The Fries rearrangement of benzoyl esters of the naphthols is of some interest in view of the value of hydroxy ketones as intermediates for the preparation of benzanthrone derivatives. This is described in a patent by Meister, Lucius, and Bruning.

There has been much controversy concerning the mechanism of the Fries reaction. It was at first considered to be an intramolecular rearrangement, but from the results of the action of aluminum chloride upon mixtures of aryl esters, Rosenmund and Schnurr suggested that the reaction must be bimolecular. A mixture of p-cresyl benzoate and o-chloro-p-cresyl acetate gave all four possible products when heated to 150° with aluminum chloride. The subsequent work of Rosenmund and Lohfert, reported in Berichte *61*, 2601 (1928), was also in accord with this mechanism. Auwers and co-workers, however, could not explain their results upon this basis, as shown in Berichte *61*, 416, 1495 (1928); Ann. *464*, 293 (1928). It has been demonstrated recently by Cox in J. Am. Chem. Soc. *52*, 352 (1930) that it is possible to obtain acetyl chloride by the action of aluminum chloride upon 2,4,6-trichlorophenyl acetate. This suggests that the first stage of the Fries reaction is an analogous reaction, followed by ketone formation due to the reaction of the acid chloride with the aluminum salt, ($C_6H_5OCOCH_3 + AlCl_3 \rightarrow C_6H_5OAlCl_2 + CH_3COCl$). This theory is, however, difficult to reconcile with the fact that the action of aluminum chloride and an acid chloride upon a phenol according to the Friedel-Craft method gives in some instances a different product than that resulting from the Fries reaction.

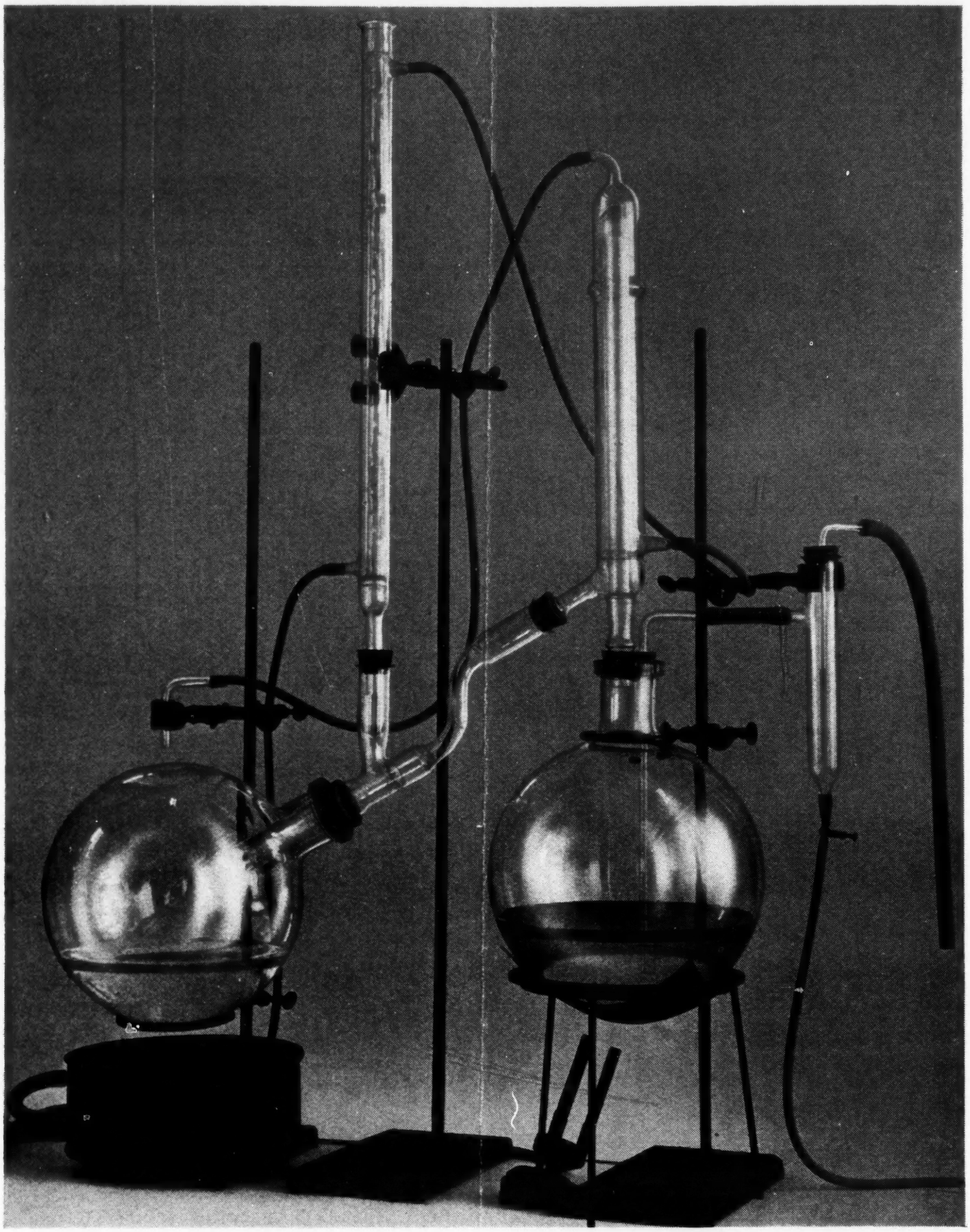
Thus, the Fries reaction is another example of the remarkable utility of aluminum chloride in bringing about organic reactions. In this case it is of considerable value from the standpoint of synthesis, and is likewise of theoretical interest because of the still somewhat uncertain mechanism involved.

Diphenylthiocarbazone
A New Reagent for Heavy Metals

ONE of the newest additions to the list of Eastman Organic Chemicals is diphenylthiocarbazone. This compound has attracted much attention on account of its sensitive color reactions with traces of heavy metals. Diphenylthiocarbazone seems to be effective not only with metallic salts, but also with more stable combinations such as oxides and sulfides, as well as the metallic elements themselves.

The reagent consists of a solution containing about 4 mg. of diphenylthiocarbazone dissolved in 100 c.c. of chloroform or carbon tetrachloride. The solution has a distinct green color. When this reagent is shaken with an aqueous solution containing a trace of mercury, an orange-colored complex is formed which dissolves in the chloroform layer. With copper, in weakly ammoniacal solutions, a yellow-brown coloration results which changes to violet on acidification.

The complex formed with lead salts is a salmon-red color and is particularly suitable for quantitative estimation of small amounts. The U. S. Department of Agriculture recommends a procedure using diphenylthiocarbazone for detecting the traces of lead residues on fruits that have been treated with sprays containing lead compounds.



Compact Steam Distillation Set-up

IN a laboratory where desk space is at a premium, the usual steam distillation set-up, with its long condenser, takes more than its share. For this reason, the compact set-up illustrated above is particularly useful. It is designed with efficient vertical condensers for maximum condensation, and requires a minimum of desk area. The steam inlet is through the trap on the right.

Eastman Organic Chemicals as Analytical Reagents

XXXII MERCURY

p-DIMETHYLAMINOBENZAL-RHODANINE

Kolthoff, J.A.C.S. *52*, 2222 (1930)

Weakly acid solutions of mercurous mercury give a red precipitate with a saturated alcoholic solution of the above compound (10 c.c. mercury solution + 0.5 c.c. 4N Nitric Acid + 0.3 c.c. reagent). Mercury concentrations of 1 mg. per liter give a faintly red coloration, while the limit of sensitivity is 0.5 mg. per liter. Mercurous mercury reacts even in the presence of chloride since the rhodanine compound is less soluble than mercurous chloride. Under the same conditions mercuric mercury in well dissociated mercury salts gives a red color or precipitate with the reagent, the sensitivity being 0.2 mg. per liter with mercuric nitrate. Addition of chloride or bromide decreases the sensitivity very much. Silver interferes as it also yields a red color or precipitate.

PROPYLENEDIAMINE

Spacu and Spacu, Z. ANAL. CHEM. *89*, 188 (1932)

The reagent is prepared by dissolving 2.5 grams of crystalline copper sulfate in water, then adding 2 grams of a 70-75% solution of propylenediamine. It should be made up at the time it is needed. The method depends on the formation of a precipitate having the composition $HgI_4 \cdot Cu(pn)_2$ and containing 21.81% mercury. 100 to 200 c.c. of the mercury solution (about 0.3 gram Hg), which should be neutral or slightly ammoniacal, is mixed with an excess of potassium iodide, and heated almost to the boiling point. It is then mixed with a boiling hot solution of the above reagent, also in excess. On cooling thoroughly, dark blue-violet crystals separate, and are filtered on a porcelain crucible. The precipitate is washed 3 to 6 times with an aqueous solution containing 0.1% KI and 0.1% $Cu(pn)_2SO_4$. It is then washed 3 to 4 times with 2 c.c. of 96% alcohol, and finally washed 2 to 4 times with 2 c.c. of ether. It is then dried in a vacuum desiccator, and weighed.

DIPHENYLTHIOCARBAZONE

Wolbling and Steiger, ANGEW. CHEM. *46*, 279 (1933); Fischer, ANGEW. CHEM. *46*, 442 (1933)

Diphenylthiocarbazone is a sensitive reagent for estimating traces of mercury colorimetrically. A solution is used containing 2 to 4 mg. of the reagent dissolved in 100 c.c. of chloroform. Mercury salts form an orange complex which remains in the chloroform layer, and, after suitable treatment, can be compared in a colorimeter with known standards. The effects of disturbing ions are discussed, and methods given for the determination in their presence.

PYRIDINE

Korenman, PHARM. ZENTRALHALLE, *74*, 54 (1933)

Mercury and a number of other heavy metals form compounds with pyridine and dichromate which are only slightly soluble. The precipitates form definite crystalline compounds which may be used for microchemical identification.

New Eastman Organic Chemicals

3092	Diphenylthiocarbazone	10 gm.	$3.00 A
3612	Ethyl Suberate BP 146-149°/6 mm.	10 gm.	3.50 A
P 3613	Methyl Chloroform (Pract.) BP 74-76°	1 kg.	5.00 E
P 3614	as-Dichloroethylene (Pract.) BP 33-35°	1 kg.	3.75 E